Advancing Clinical Improvements for Patients Using the Theory-Driven and Data-Driven Branches of Computational Psychiatry

Huys, Quentin J M

Abstract: The brain is special: it computes. Which computations the brain is able to perform is determined both by its biology but also by the history of computations the brain has performed. An inability by the brain to compute adaptive solutions to the problems it faces can therefore give rise to mental illness both through mechanisms akin to those in other areas of medicine, such as cellular dysfunctions, but also through the consequence of "ill-learning," for instance, after traumatic events. This line is blurry: illness can obviously give rise to ill-learning and ill-learning to illness, eg, through substance abuse often seen after trauma.

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VIEWPOINT

Advancing Clinical Improvements for Patients Using the Theory-Driven and Data-Driven Branches of Computational Psychiatry

Quentin J. M. Huys, MD, PhD
Centre for Addictive Disorders, Department of Psychiatry, Psychotherapy and Psychosomatics, Hospital of Psychiatry, University of Zürich, Switzerland; and Translational Neuromodeling Unit, Institute for Biomedical Engineering, University of Zürich and Swiss Federal Institute of Technology, Zürich, Switzerland.

Corresponding Author: Quentin J. M. Huys, MD, PhD, Translational Neuromodeling Unit, Wilfriedstrasse 6, 8032 Zürich, Switzerland (qhuys@cantab.net).

The brain is special: it computes. Which computations the brain is able to perform is determined both by its biology but also by the history of computations the brain has performed. An inability by the brain to compute adaptive solutions to the problems it faces can therefore give rise to mental illness both through mechanisms akin to those in other areas of medicine, such as cellular dysfunctions, but also through the consequence of "ill-learning," for instance, after traumatic events. This line is blurry: illness can obviously give rise to ill-learning and ill-learning to illness, eg, through substance abuse often seen after trauma.

Computational psychiatry is a young and dynamic field whose unique contributions are that it directly addresses the fundamental computational nature of brain function and renders highly complex data and phenomena tractable. It is a highly interdisciplinary field that draws on machine learning, neuroscience, psychology, and psychiatry. In its theory-driven guise, it uses mathematical and statistical methods to understand the unmet computational needs underlying psychiatric illnesses.[1] This involves building formal models of specific processes at 3 partially independent levels of analysis.[2] The levels describe the nature of the computational problems the brain faces, the algorithm it uses to solve them, and how the algorithms are implemented. In its data-driven form, it uses mathematical and statistical methods to identify clinically useful patterns in complex, often high-dimensional, data sets.

This Viewpoint is part of a series on pragmatic evidence-based psychiatry[3] that arises from the tangible disillusionment with the speed at which explanatory advances in our understanding of the brain have been translated into clinical improvements for patients. Here, I argue that both theory-driven and data-driven branches of computational psychiatry can advance this pragmatic agenda.

Strictly speaking, explanatory research in the sense of theory and understanding is neither necessary nor sufficient for treatment: pragmatic evidence-based medicine is replete with treatments that are effective but whose mechanisms of action remain unknown. Paracetamol, clozapine, and electroconvulsive therapy are but a few examples. However, the current diagnostic conundrum is witness to the fact that the theory-free evidence-based approach has not provided a fruitful framework for the development of novel therapies. While it correctly describes aspects of the correlational structure of psychiatric symptoms and captures severity in a clinically useful way, it confounds the multiple underlying cognitive and neurobiological causes. As has been recognized by the National Institute of Mental Health Research Domain Criteria, adhering to this framework impedes progress on identifying the causes of mental illness and obscures targets for interventions. Theory-driven explanatory computational modeling is uniquely placed to carve the brain's computational nature at its joints, characterize relevant processes, and identify targets for intervention. For instance, network models of symptoms[4] allow us to reconceptualize the notion of latent classes, opening entirely new avenues to target interventions. Other examples are the characterization of cognitive processes to target with cognitive modifications[5] and of task-related neural activations to target through neurostimulation, eg, the neural arbitrators between different decision processes[6] (see also Viewpoint by Etkin[7]).

A specific tool from theory-driven computational psychiatry worth mentioning here is generative modelling. This produces simulated data sets that are akin to the raw data obtained in an experiment. Several features make such simulations useful pragmatic tools. First, they allow measurement of unobserved neural and cognitive processes in unparalleled detail.[8] Second, statistically inverting these models involves fitting the parameters such that the generated data resemble that observed. These parameters thereby function as sufficient statistics, succinctly describing the data and hence measuring complex phenomena. Third, generative models increase robustness, reproducibility, and generalizability by allowing for quantitative assessments of model complexity through processes such as Bayesian model comparison. A parsimonious generative model mostly generates data similar to the observed data in the experiment, irrespective of its parameter settings. A model that overfits only rarely produces such data, ie, only for a narrow range of its parameters. Generative modeling is very unlike standard approaches to data analysis, which involve focusing on often very narrow aspects of the data and applying general-purpose statistical tests to these statistics. Because data can often be sliced in many ways, such partial tests often imply very complex models and overfitting, which will reduce replicability and generalizability.

Machine learning provides powerful data-driven tools to discover clinically useful patterns in complex data sets.[9] Conceptually, it involves a shift in emphasis away from testing differences in the mean of distributions toward predicting individual outcomes accurately. Clearly, the latter has more translational potential. It is incumbent on the field to put these novel statistical approaches to work on novel and existing data.[9] From both a pragmatic and ethical viewpoint, it appears imperative to attempt to pool existing clinical trial data to examine whether machine-learning tools could deliver treatment response prediction and treatment selection tools. One strength of machine-learning prediction approaches is their agnostic nature; nearly any data will do. However, this strength can also be a substantial weakness because it underpins the requirement for large data sets. It can also result in highly complex answers that are not transparent, and its data-hungry nature poses important privacy problems. Theory-driven tools can come to help: when the parameters of theory-driven models are sufficient statistics, they capture the fundamental patterns driving complex observations and therefore are an ideal dimensionality reduction tool that may maximise the power of data-driven tools.[1]

However, even useful tools can be put to bad use, and modeling can raise interesting questions that are irrelevant to clinical practice. To actually improve mental health, computational psychiatry research has to hone in on the targets identified by patients, clinicians, and stakeholders.[3] In addition, it has to focus on providing actionable information. This means that computational psychiatry investigations should probably mostly be performed in the setting of clinical care and be related to specific interventions and individual outcomes longitudinally in clinically relevant populations. Next, computational psychiatry tools require substantial expertise. To address this, publications should contain and report on the measures as complete packages (eg, task, protocols, models, and fitting routines). These complete packages could then be moved forward by subjecting them to robustness assessment and further evaluations in a series of steps within a modified developmental pathway inspired by drug development.[10]

Finally, computational psychiatry also provides useful expertise. First, mobile health, the increasing availability of sensors, and neuroimaging and cognitive probes provide complex data sets. Literacy in mathematics, statistics, data analysis, and programming will help practitioners make the most of these rich data sources. Second, the process of actually building models, generating data from them, fitting them to data, and comparing the data they generate with real data is a useful intellectual process because it forces assumptions to be made explicit and brings all their sometimes hidden and complex consequences to the fore.

Theory-driven approaches are necessary to discover novel targets and interventions. They also provide measures and efficient summaries of complex data, particularly through generative modeling. Data-driven tools enable the extraction predictive relationships between data and relevant outcomes. Their combination has the potential to improve prognostic accuracy, treatment response prediction, treatment selection, repurposing, and monitoring. Therefore, both data-driven and theory-driven approaches have pragmatic potential.

ARTICLE INFORMATION

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